



4164-01-P

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **Food and Drug Administration**

**[Docket No. FDA-2019-N-4763]**

#### **Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Assessment of Terms and Phrases Commonly Used in Prescription Drug Promotion**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

**DATES:** Submit written comments (including recommendations) on the collection of information by **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**.

**ADDRESSES:** To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to <https://www.reginfo.gov/public/do/PRAMain>. Find this particular information collection by selecting “Currently under Review--Open for Public Comments” or by using the search function. The title of this information collection is “Assessment of Terms and Phrases Commonly Used in Prescription Drug Promotion.” Also, include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** Ila S. Mizrachi, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-7726, [PRAStaff@fda.hhs.gov](mailto:PRAStaff@fda.hhs.gov).

*For copies of the questionnaire, contact:* Office of Prescription Drug Promotion (OPDP) Research Team, [DTCresearch@fda.hhs.gov](mailto:DTCresearch@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:** In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Assessment of Terms and Phrases Commonly Used in Prescription Drug Promotion

OMB Control Number 0910-New

## I. Background

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes FDA to conduct research relating to health information. Section 1003(d)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(d)(2)(C)) authorizes FDA to conduct research relating to drugs and other FDA regulated products in carrying out the provisions of the FD&C Act.

The Office of Prescription Drug Promotion's (OPDP) mission is to protect the public health, in part, by helping to ensure that prescription drug promotional material is truthful, balanced, and accurately communicated, so that patients and health care providers can make informed decisions about treatment options. OPDP's research program provides scientific evidence to help ensure that our policies related to prescription drug promotion will have the greatest benefit to public health. Toward that end, we have consistently conducted research to evaluate the aspects of prescription drug promotion that are most central to our mission. Our research focuses in particular on three main topic areas: advertising features, including content

and format; target populations; and research quality. Through the evaluation of advertising features, we assess how elements such as graphics, format, and disease and product characteristics impact the communication and understanding of prescription drug risks and benefits. Focusing on target populations allows us to evaluate how understanding of prescription drug risks and benefits may vary as a function of audience, and our focus on research quality aims at maximizing the quality of our research data through analytical methodology development and investigation of sampling and response issues. This study will inform all three topic areas.

Because we recognize that the strength of data and the confidence in the robust nature of the findings is improved by utilizing the results of multiple converging studies, we continue to develop evidence to inform our thinking. We evaluate the results from our studies within the broader context of research and findings from other sources, and this larger body of knowledge collectively informs our policies as well as our research program. Our research is documented on our homepage, which can be found at:

<https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm090276.htm>. The website includes links to the latest *Federal Register* notices and peer-reviewed publications produced by our office. The website maintains information on studies we have conducted, dating back to a survey on direct-to-consumer advertisements conducted in 1999.

The present research involves assessment of how consumers and primary care physicians (PCPs) interpret terms and phrases commonly used in prescription drug promotion, as well as those used to describe prescription drugs and prescription drug promotion more generally. This includes both what these terms and phrases mean to each population (e.g., definitions) and what these terms and phrases imply (e.g., about efficacy and safety). Some examples of interest include: “natural” or “naturally-occurring,” and “targeted” or “targeted therapy.” The full list for

assessment will include approximately 30 terms and phrases for each population. To accommodate such a large number, presented terms and phrases will be accompanied by only limited context (terms within sentences and phrases within paragraphs, as opposed to full promotional materials). Understanding the most prevalent interpretations of these terms and phrases can help OPDP determine the impact of specific language in prescription drug promotion. For example, certain terms and phrases, when used without additional contextual information, might overstate the efficacy or minimize the risk of a product. Additionally, from a health literacy perspective, it is helpful to ascertain general understanding of such terms and phrases as this may aid in the development of best practices around communicating these concepts.

We plan to conduct this research in two phases. First, we will conduct formative semi-structured interviews with 30 members of each population (general population consumers and PCPs). Second, we will conduct nationally representative, probability-based surveys of more than 1,000 members of each population on the same topic.

*Phase 1: Semistructured Interviews.* In Phase 1 of the research, semistructured interviews will be conducted by web conferencing using the itracks platform, an online and mobile market research service provider. This approach allows for the participant and interviewer to see each other and includes a whiteboard feature that can be used to show the terms, statements, or passages for participants to read and follow along as the interviewer reads them aloud. This may be helpful in cases where the statements or passages are long, which may make them difficult to understand when read aloud. In addition, the written information may be helpful as a reference as the discussion progresses.

Participation is estimated to take 1 hour. Participants will be recruited by email through itracks and its partner panels. All participants will be 18 years of age or older and must not have participated in a focus group or interview during the previous 3 months. Additionally, for the consumer sample, we will exclude individuals who work in healthcare or marketing settings because their knowledge and experiences may not reflect those of the average consumer. For the PCP sample, we will exclude individuals who spend less than 50 percent of their time on patient care. Department of Health and Human Services employees and RTI International employees will be excluded from both respondent groups.

We will start data collection with a soft launch of three interviews per segment (10 percent) to ensure that all processes are working well. Although we do not intend on making major changes to the interview guides as a result of these soft launch interviews, they will provide an opportunity to make minor changes (e.g., adding interviewer notes). Measurement for this phase will consist of a thematic analysis using a matrix approach to identify themes and mental models common across participants.

*Phase 2: Nationally Representative Surveys.* In Phase 2 of the research, primarily closed-ended survey questions will be administered to each population. The closed-ended survey format will allow the team to quantify the frequency or prevalence of certain interpretations or meanings among a nationally representative sample of the general U.S. consumer and physician populations. Final questions and response options will be informed by key interpretations discovered during the Phase 1 interviews. For the consumer survey, we will use a probability sample selected from an address-based sampling frame and conduct the survey using a web-based platform. For the PCP survey, we will obtain a probability sample from the American Medical Association Masterfile and will conduct the survey via mail. For each

population, we chose the sampling frame and survey mode that has been shown to produce the highest quality results for that population with respect to coverage, response rates, and nonresponse bias. The same exclusion criteria as specified for Phase 1 will be maintained for Phase 2. Participation is estimated at 20 minutes.

We also plan to embed an experiment in the PCP mail survey. Research has shown that including a pen in the survey package can help to increase response rates and time to response, even potentially reducing the number of reminders required (Refs. 1 and 2). However, the shipping of pens can be costly and often pens are damaged in the mail (e.g., ink can leak, etc.). To determine whether another token incentive might be as effective at increasing response rates, we will randomize half of the sample to receive a pen and half to receive a packet of sticky notes or other token incentive. We will compare response rates between the two groups to help inform methods for future studies.

We set our sample requirements to a 95 percent confidence interval and a 3 percent margin of error assuming an underlying proportion of 0.50 in the population (which is the most conservative estimate and overestimates the sample size relative to alternate proportions). These parameters are commonly used in quantitative survey research (Refs. 3 to 6) and offer balance between precision and cost. Thus, assuming a total U.S. population of roughly 250 million adults aged 18 or older (Ref. 7), we estimate the number of completed surveys to be 1,067 for the general population survey. Assuming a total population of 209,000 PCPs (Ref. 8), with the same 95 percent confidence interval and  $\pm 3$  percent margin of error, we estimate the number of completed surveys for the provider survey to be 1,062. These sample sizes would also allow us to detect a mean difference between  $\pm 0.15$  and 0.30 points (Ref. 6).

In the *Federal Register* of November 6, 2019 (84 FR 59833), FDA published a 60-day notice requesting public comment on the proposed collection of information. FDA received eight comments, but only five submissions were PRA-related. Within those submissions, FDA received multiple comments that the Agency has addressed.

(Comment 1) Some comments supported the proposed research as an important step towards addressing current issues with U.S. prescription drug advertisement practices.

(Response) FDA agrees with these comments to the extent they relate to this study.

(Comment 2) A few comments suggested the proposed research methodology could be improved by providing the general population with the option to complete the survey in writing or over the phone. These comments asserted that elderly consumers are highly susceptible to false and misleading advertisements of prescription drugs, and that elderly consumers use prescription drugs at rates higher than any other age group. The comments also indicated that elderly populations may face barriers to accessing a web-based platform to complete the survey.

(Response) While we agree that web panel surveys can sometimes have less than ideal coverage of populations like older adults, the survey proposed here would not be sampling from a web panel, but would instead use a probability sample selected from an address-based sample frame to ensure a nationally-representative sample. This helps to ensure better coverage of older adults, who may be less likely to be part of an existing opt-in survey panel or less likely to answer a web-based ad to complete a survey than to respond to a mailed survey invitation. Pew research finds that 73 percent of people aged 65+ have access to the internet in their home compared to 90 percent for the overall U.S. population (Ref. 9). To address this coverage concern, responses from older adults will be weighted to the full U.S. population.

Our recent experience suggests we will be able to adequately represent this group. As an example, in a survey conducted by RTI on the Residential Energy Consumption Survey National Pilot, an analysis of representativeness among survey protocols found that for the older age group, web was less representative than a mixed mode survey allowing for either web-based or paper survey, but was still considered to have “good” agreement with the American Community Survey (considered the gold standard for U.S. demographic data).

(Comment 3) The comment indicated the proposed research methodology could be improved by including behavior-based questions in the surveys.

(Response) We agree about the value of measuring behavioral intentions in general. However, in this particular study, in which we are asking about a variety of terms and phrases used in prescription drug advertising that may or may not be relevant to all members of the sample, behavioral intention questions would not be appropriate. The drugs in question would not be relevant or salient for all consumers in the study. For example, a respondent will be able to answer questions about language used to describe migraine medication (e.g., #1 prescribed medication) even if they do not suffer from migraines. However, it would not make sense to ask them about their behavioral intentions related to taking that migraine medicine if they do not suffer from migraines. Given the limitations of space and scope, we do not plan to add more behavioral intentions measures into this study.

(Comment 4) The comment suggested that some of the longer contextual-based passages interviewees are presented with should include situations in which viewers/listeners are presented with previously seldom-used or new-to-the-public terms and phrases and an attempt at definition or generation of emotional valence by marketers.



(Response) The purpose of this study is for FDA to test understanding of terms “commonly used in prescription drug promotion.” Thus, those that have been “previously seldom-used” or are “new-to the-public” are outside the scope of the study and are not included in the survey materials.

The idea to study emotional valence is very interesting, but also beyond the scope of the current research.

(Comment 5) The comment included a note on the PCP mail surveys: rather than focusing on incentivizing response via an object included with the PCP mail surveys, the comment suggested that research funds would be better spent ensuring the surveys are engaging, easily understood by the two target audiences, short to complete, and presented with a clear deadline.

(Response) We believe we have the capacity both to incentivize the response and to ensure the surveys are engaging. For example, we specifically designed the advance mailings (letters that will go to potential participants) to follow best practices for ensuring the study is engaging, such as stating the purpose and likely outcomes of the research in the letter and including a graphic to identify the study on the postcard or envelope.

Token incentives have been shown in the literature to have a real impact on response rates (Refs. 1 and 2), and increased response rates can save costs and potentially reduce nonresponse bias (if reluctant respondents are different from non-reluctant respondents). In fact, the literature has shown that even with short, engaging surveys, these types of token incentives can substantially boost response rates (Refs. 10-12).

(Comment 6) The comment suggested that the study population of healthcare providers should be expanded to include specialists.

(Response) While we understand that some of the topics may be relevant for specialists, and we do often include specialists in our research, our focus in the present research is on PCPs. Specialists are not as numerous as PCPs, which makes them harder to recruit. In 2018, for example, the proportion of specialists representing each specialty area ranged from 2 percent (endocrinologists) to 11 percent (psychiatrists and emergency medicine specialists) (Ref. 13). These data demonstrate that the pool of potentially eligible specialists is limited. Given the large required sample size for this study, we chose to limit the population to PCPs.

(Comment 7) The comment suggested that FDA should use additional context for certain terms to more accurately represent the way in which these terms are conveyed in promotion. Specifically, the comment requested that FDA add context for the following terms:

1. HCP assessment term of “significant (as in statistically significant)”: the comment stated that this term should be accompanied by a 95 percent confidence interval, hazard ratio, and p-value as additional data points.
2. HCP and consumer assessment phrases “manageable safety profile; established safety profile; well-studied safety profile; “well-tolerated”: the comment stated that these phrases should be accompanied by an example, such as a table showing most common adverse events.

(Response) Regarding the term “significant (as in statistically significant)” and the suggestion to add additional data points: although references to statistical significance in the prescription drug promotion marketplace are sometimes accompanied by other statistical information, at other times they are not. In this assessment, we wish to assess understanding of this phrase on its own.

Regarding “manageable safety profile” and related phrases and the suggestion to add an example such as a table showing most common adverse events: given the length of the current instruments, we are limited in what can be included. The scope of this study includes terms and phrases and not graphics or numbers. However, we recognize the importance of studying those features as well. Examples of research involving these features can be found on the OPDP research website, linked earlier in this document.

(Comment 8) The comment suggests that the following commonly used terms should be added to the assessment to increase the utility, quality and clarity of the information collected.

For consumers and HCP, the comment suggested adding:

1. “Potent” to assessment term “powerful,” and
2. New assessment term “convenient/straightforward/simple/easy/easy to use.”

For HCPs only, the comment suggested adding “high affinity.”

(Response) Thank you for these suggestions. We added “potent,” “convenient,” “straightforward,” “simple,” “easy”, and “easy to use” to the surveys. For “high affinity,” we have conducted several informal searches, but have not found sufficient examples of the use of this term in promotional materials.

(Comment 9) The comment noted that the surveys take terms and phrases out of context and suggests that FDA should study how consumers and PCPs interpret representative promotional pieces that include appropriate accompanying context.

(Response) This study is one in a program of related research conducted by OPDP. In several related studies, we examine how consumers and PCPs interpret the terms and phrases in representative promotional pieces that include accompanying context. In contrast to this prior research, the proposed research allows for assessment of a large number of terms and phrases--

effectively emphasizing breadth over depth, and involving data collection from a nationally representative sample. We believe these various approaches to studying language commonly used in prescription drug promotion complement one another and together contribute to a more comprehensive understanding of the research questions.

(Comment 10) The comment suggested that questions in the surveys may be leading. In describing the proposed research, the 60-day notice stated, “For example, certain terms and phrases, when used without additional contextual information, might overstate the efficacy and minimize the risk of a product.” The comment stated that this statement shows bias that manifests in the proposed questions and suggests that because the evident bias is deeply rooted in this proposed study and its surveys, FDA should fundamentally reformulate the proposed collection of information in its entirety.

(Response) We agree that some of the probes proposed for use in the Phase 1 research may appear to be leading, so we have rewritten these probes. For example, where it said “safer,” we have altered language to “more” or “less” safe.

In the Phase 2 surveys, the safety and efficacy questions are not leading or one-sided. The questions use bipolar response scales allowing respondents to indicate that the products using that term are less safe/effective, equally as safe/effective, or more safe/effective.

(Comment 11) The comment suggested that the proposed answers in the closed-ended surveys are unbalanced.

(Response) We have reviewed the Phase 2 questions and made some edits to ensure more balance.

It is important to note that the response options shown for many of the questions are just examples. The full list of response options used in the Phase 2 surveys will be developed based

on responses to the Phase 1 interviews. As a result, the Phase 2 response options may skew slightly negative or positive depending on what interview respondents say in the Phase 1 interviews. However, we will ensure that there is balance with both negative and positive response options.

(Comment 12) The comment suggested that by asking respondents to compare closely related terms and phrases, the survey may force artificial findings of difference. The comment stated that even if the measured differences are real (and not due to biases in the surveys), it is unclear how the results would have any practical utility because there may not be any objective definitions of the terms with which to compare the results.

(Response) We describe below the process to mitigate the effects of this concern.

- If participants in the Phase 1 research do not articulate differences between certain terms, we will exclude those terms from Phase 2. This will reduce the chance to find artificial differences between terms.
- We can also split question sets into multiple individual questions. We will make decisions surrounding this solution following completion of the Phase 1 interviews.
- For the consumer survey, which will be conducted online only, we will randomize the order in which the terms are presented. This will not eliminate context effects but will randomly distribute any error across terms rather than significantly biasing an individual term.

(Comment 13) The comment opined that the surveys, at least in the past, are unnecessarily duplicative of information otherwise reasonably accessible to FDA (e.g., focus groups conducted by FDA in 2014; and information available from third-party sources regarding the terms “many,” “most,” “majority,” “some,” and “few”).

(Response) We believe the research is not duplicative of that conducted in 2014 by FDA, but instead builds on that research. It is being conducted by the same research team and is part of a coherent program of research that includes formative focus groups, in-depth interviews, a survey, and an experimental study. We used those focus group reports to inform the development of answer options for this study. The very few terms that are repeated in the current survey have been included in the current study because researchers wanted to follow up on previous findings with a larger, nationally representative sample. Furthermore, that study did not collect any quantitative data on the terms.

Literature searches in multiple medical, social science, and linguistics databases, including Pubmed, Web of Science, EBSCO Discovery Service, and Linguistics Database for research on how people quantify or interpret terms like “few” and “many” as we do in the present research did not reveal significant literature on these terms. It is important for FDA to understand how these terms are interpreted in the context of prescription drug promotion, thus we plan to keep them in the current study.

(Comment 14) A comment recommended that FDA remove questions about the terms “off-label” and “prescription drug promotion” as they are not terms used in promotion.

(Response) While “off label” and “prescription drug promotion” are not terms that are typically used in promotion, it is important for FDA to understand how healthcare providers perceive these terms in general. We have revised the description of the scope in the *Federal Register* notice to clarify this broader purpose. We now state: “The present research involves assessment of how consumers and primary care physicians (PCPs) interpret terms and phrases commonly used in prescription drug promotion, as well as those used to describe prescription drugs and prescription drug promotion more generally.”

(Comment 15) A comment recommended that FDA change the framing for the survey from a focus on “words or phrases that are commonly used in prescription drug advertising” to “words or phrases that are commonly used to describe prescription drugs.” The comment suggested that if the survey keeps the former, respondents will view the surveys through whatever biases they have for drug advertising.

(Response) Because it is our intention to examine what participants think in the context of prescription drug advertising, we have retained our original approach to framing the research, while also expanding that framing to reference terms or phrases that are commonly used to describe prescription drug promotion.

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden<sup>1</sup>

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
<i>General Population</i>					
Phase 1: screener completes (assumes 35% eligible)	85	1	85	0.083 (5 minutes)	7
Phase 1: number of completes	30	1	30	1	30
Phase 2: screener completes (assumes 90% eligible)	1,185	1	1,185	0.083 (5 minutes)	98
Phase 2: number of completes	1,067	1	1,067+10% <sup>2</sup> = 1,174	0.333 (20 minutes)	391
<i>PCP Population</i>					
Phase 1: screener completes (assumes 30% eligible)	104	1	104	0.083 (5 minutes)	9
Phase 1: number of completes	30	1	30	1	30
Phase 2: screener completes (assumes 90% eligible)	1,180	1	1,180	0.083 (5 minutes)	98
Phase 2: number of completes	1,062	1	1,062+10% <sup>2</sup> = 1,168	0.333 (20 minutes)	389
Total					1,052

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

<sup>2</sup> As with most online and mail surveys, it is always possible that some participants are in the process of completing the survey when the target number is reached and that those surveys will be completed and received before the survey is closed out. To account for this, we have estimated approximately 10 percent overage for both samples in the study.

## II. References

The following references marked with an asterisk (\*) are on display at the Dockets Management Staff (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at <https://www.regulations.gov>. References without asterisks are not on public display at <https://www.regulations.gov> because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

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Dated: September 14, 2020.

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[FR Doc. 2020-20621 Filed: 9/17/2020 8:45 am; Publication Date: 9/18/2020]